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Ischemic preconditioning and the risk of acute kidney injury

To the Editor: We have read with interest the paper by Zimmerman *et al.*,[1] in which the authors randomized to either ischemic preconditioning or no intervention 120 patients undergoing cardiac surgery. The authors reported a marked 57% lower risk for acute kidney injury (AKI) in patients in whom preconditioning occurred.

Such a result may be partly explained by the study being underpowered. The authors reported that a total of 120 subjects would provide 62% power to detect a 50% reduction in the risk of AKI. The main concern with underpowered studies is the increased risk of type II error (failing to reject a false null hypothesis). However, an often underlooked problem arising from underpowered studies is the increased risk of type I error (failing to reject a true null hypothesis).[2] In particular, simulation studies have shown how studies with low power tend to yield incorrectly inflated effect size estimates.[3]

1. Zimmerman RF, Ezeanuna PU, Kane JC *et al.* Ischemic preconditioning at a remote site prevents acute kidney injury in patients following cardiac surgery. *Kidney Int* 2011; **80**: 861–867.
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The Authors Reply: We appreciate the opportunity to address concerns regarding statistical power in our study.[1] Ferraro and Gambaro's[2] statement that underpowered studies are at increased risk for type I error is, in our opinion, an oversimplification of a rather complex issue. It can be argued that equal *P*-values represent equal risks for type I error regardless of sample size, or even that lower statistical power strengthens the evidence represented by a given *P*-value and reduces the likelihood of type I error.[3] As we found an effect of remote ischemic preconditioning that was highly statistically significant ($P = 0.004$), we consider it improbable that ours was a 'false-positive' study.

The authors raise the valid point that because small, underpowered studies require more extreme results to reach statistical significance, they tend to overestimate effect size. We regret not acknowledging this issue in our discussion of limitations. Our *a priori* power analysis was based on pilot data. If the observed data in our study are 'true', then the power to detect the observed differences is substantially higher than the 62% estimated before the study started, and is rather 83%. At 60% power, the simulation studies reported by La Caze, *et al.*[4] indicate that the probability of significant result bias is quite low, and at 80% power 'shrinks to negligible levels'. We therefore consider it unlikely that our findings are seriously biased *vis-à-vis* the effects of low statistical power.

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Biomarker for interstitial inflammation

To the Editor: Zhang *et al.*[1] have conducted a proof-of-concept cross-sectional study on biomarkers of interstitial inflammation in lupus nephritis. Although the authors allude to biomarkers leading to a 'continuous readout of kidney pathology', they use a dichotomous gold standard (none–mild vs. moderate–severe interstitial inflammation on histology). It would be more informative to observe the four groups separately as classified by the blinded nephropathologist. Was there a gradient (dose–response) in the levels of biomarkers in the four groups of none, mild, moderate, and severe? This may not be 'clinically significant' but will increase confidence in the result.